POSTER #EE488

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A SYSTEMATIC REVIEW ON ECONOMIC EVALUATIONS OF DISEASE MODIFYING INTERVENTIONS FOR ALZHEIMER'S DISEASE

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Summary

Ageing population drives pressing need for effective Alzheimer's disease (AD) intervention. New disease modifying agents offers hope at steep price tag.

- We reviewed published studies to provide insights on value demonstration of such therapies and potential value pricing for impending pipeline.
- A total of 8 studies from 2017 and 2022 reporting Aducanumab (n=4), Donanemab (n=1), Lecanemab (n=1), hypothetical disease modifying agents (n=3)

None of disease modifying agents showed cost-effectiveness at current prices, ICER values were most sensitive to treatment efficacy, suggesting that future disease modifying therapies must justify their high costs to be considered cost-effective.

Population

Patients with mild cognitive impairment from AD to mild to severe AD.

Setting: United States
Horizon: Lifetime

Introduction

Disease modifying therapies for Alzheimer's disease (AD) have the potential to significantly alter the treatment paradigm. However, the clinical potential should pair with appropriate prices to ensure value is delivered. This study reviews the current landscape of potential disease modifying agents in development and evidence on their economic value in treating patients with mild to severe AD.

Objective

- Review available passive immunotherapies in market or in development for patients with mild to severe AD.
- Analyse the cost-effectiveness of passive immunotherapies and hypothetical disease modifying agents in patients with mild to severe AD.

Methodology

We conducted a systematic review of economic evaluation studies on passive immunotherapies or hypothetical disease modifying agents in the treatment of AD. Active immunotherapies, although in development, were excluded from the review given the relative infancy of their development.

Approach

- Studies published between 2017 and 2022 were identified using PubMed and Embase.
- Key terms included in the search: Alzheimer, Aducanumab, Lecanemab, Donanemab, Solanezumab, Crenezumab, Gantenerumab, disease modifying, cost effectiveness, cost utility, cost benefit, cost consequence, economic evaluation, economic modeling.

Inclusion Criteria

- Full economic evaluations
- Studies published in English
- Patients with mild to severe AD
- Passive immunotherapies or disease modifying agents that are approved or in development

Key Data Points

- Intervention and relevant comparators
- Perspective
- Type of analysis (cost utility analysis, cost benefit analysis, etc.)
- Time horizon
- Key economic outcomes such as ICER values
- Key assumptions
- Patient population and disease type

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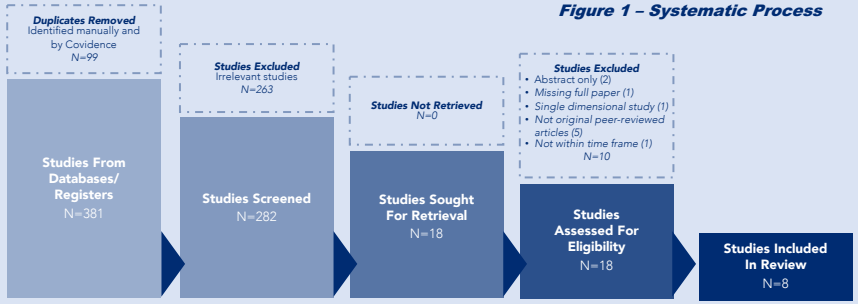
Results

- Interventions assessed: Aducanumab (n=4), Donanemab (n=1), Lecanemab (n=1), hypothetical disease modifying agents (n=3).
- The most common perspectives adopted were the healthcare system (n=6) and societal perspectives (n=6).
- Aducanemab and Donanemab were not cost effective at their proposed prices under a WTP threshold of $100,000-$150,000.
- Value based pricing for aducanumab ranging from $2,000 to $22,820 (healthcare perspective) depends treatment efficacy on halting AD
- Inclusion of caregiver QALYs made one hypothetical therapy cost effective.
- Model was most sensitive to treatment efficacy.

Figure 1 – Systematic Process



Study	Key Study Characteristics	Intervention	Type	Key Assumptions	Costs	Key Results
Synnott 2021 [3]	**Population:** Patients with mild cognitive impairment from AD or mild-severe AD **Perspective:** Healthcare, societal	1. Aducanumab + standard of care 2. Standard of care	Cost Utility	1. Treatment efficacy and costs derived from EMERGE and ENGAGE trials 2. 5 health states based on disease severity 3. Setting of care (IE community or long-term care) tracked for each state 4. Treatment discontinued upon development of severe AD	1. Annual treatment cost + 6% markup from administrative cost at $56,000 2. Key cost inputs: direct healthcare costs, productivity impacts, caregiver time, caregiver direct healthcare costs 3. Total incremental costs: $202,000 (societal)-$204,000 (healthcare)	1. Base case ICER: $1.27M (societal)-$1.33M (healthcare) 2. Value based pricing of $2,950-$5,960 (healthcare) under WTP threshold range of $100,000-$150,000
Whittington et al 2022 [8]	**Population:** Patients with mild cognitive impairment from AD or mild-severe AD **Perspective:** Healthcare, societal	1. Aducanumab + supportive care 2. Supportive care	Cost Utility	1. Treatment efficacy and costs derived from EMERGE and ENGAGE trials 2. Assumed no treatment effect from moderate AD state onwards 3. 5 health states based on disease severity 4. Treatment efficacy beyond mild dementia from AD assumed to be half of that of clinical data	1. Annual treatment cost at $56,000 2. Key cost inputs: direct healthcare costs, long-term care, patient productivity, caregiver time, caregiver medical costs, admin costs 3. Total costs for Aducanumab: $546,000 (healthcare)-$838,000 (societal) 4. Total costs for supportive care: $204,000 (healthcare)-$636,000 (healthcare)	1. Base case ICER: $1.27M (societal)-$1.33M (healthcare) 2. Value based pricing of $2,950-$3,740 under WTP threshold of $100,000
Sinha 2022 [7]	**Population:** Patients with early AD **Perspective:** Healthcare	1. Aducanumab 2. Standard of care	Cost Utility	1. Assumed that patients on aducanumab did not transition past mild AD 2. Aducanumab analyzed under a base-case scenario that halts AD progression	1. Annual treatment cost at $56,000 2. 5-year costs with aducanumab vs SOC: $255,440 vs $75,550 3. Key cost inputs: direct healthcare costs, state-specific costs	1. Base case ICER: $383,080 2. Value based pricing of $22,820 under a WTP threshold of $100,000
Tahami 2022 [6]	**Population:** Patients with early AD **Perspective:** Payer, societal	1. Lecanemab + standard of care 2. Standard of care	Other (Disease Simulation)	1. Treatment effect: 26% change from baseline CDR-SB 2. AD state transition and efficacy data derived from phase II trial data 2. Biweekly dosing beyond phase II trial timeline 3. 5 health states based on disease severity 4. Treatment discontinued upon development of moderate AD and scenario analyses with treatment durations of 1.5, 3, and 5 years	1. Key cost inputs: direct healthcare costs, indirect healthcare costs, caregiving costs 2. Health state specific costs derived from GERAS-US 3. Total non-treatment incremental cost (excluding acquisition cost): -$11,214 (societal) - -$8,7070 (payer) per person	1. Value-based pricing of $9,249-$35,605 and $10,400-$38,053 for payer and societal perspectives respectively under WTP threshold ranges of $50,000-$200,000
Ross 2022 [5]	**Population:** Patients with early AD **Perspective:** Healthcare, societal	1. Aducanumab 2. Donanemab 3. Standard of care	Cost Utility	1. AD state transition and efficacy data derived from phase II and III trial data 2. Treatment effect: disease progression hazard ratios of 0.71 and 0.69 for Aducanumab and Donanemab respectively 3. Treatment discontinued upon AB reduction or upon development of severe AD 4. 5 health states based on disease severity	1. Annual treatment costs of Aducanumab and Donanemab at $28,000 2. Key cost inputs: direct healthcare costs, unpaid caregiving costs, increased monthly healthcare and societal costs with increased disease severity 3. Total incremental costs (Aducanumab): $127,800 (societal)-$130,1000 (healthcare) 4. Total incremental costs (Donanemab): $71,600 (societal)-$78,700 (healthcare)	1. Base case ICER (Aducanumab vs soc): $964,000 (societal)-$981,000(healthcare) 2. Base case ICER (Donanemab vs soc): $176,000 (societal)-$193,000 (healthcare) 3. Value based pricing for Aducanumab and Donanemab of $2,000-$3,000 (societal, healthcare) and $17,000-$22,000 (societal, healthcare) respectively
Green et al 2019 [1]	**Population:** Patients with mild cognitive impairment from AD **Perspective:** Healthcare	1. Hypothetical agent 2. Standard of care	Cost Utility	1. Treatment effect: 20% reduction in the risk of transitioning from mild AD to more severe states 2. Treatment discontinued upon progression from mild cognitive impairment to AD dementia	1. Annual treatment cost at $5,000 2. Key cost inputs: treatment cost, cost of care such as hospitalizations and at home care (relevant cost inputs derived from Gustavsson et al 2011 [9]	1. Base case ICER: $50,542 2. Model was most sensitive to treatment efficacy
Ito et al 2022 [2]	**Population:** Patients with mild cognitive impairment from AD **Perspective:** Healthcare, societal	1. Hypothetical agent 2. Standard of care	Cost Utility	1. Treatment effect: 25% reduction in risk of changes to CDR-SB scores 1.5 years after treatment initiation 2. Treatment discontinued upon development of moderate AD dementia 3. Disease severity dictated by cognition via the MMSE	1. Annual treatment cost at $16,000 2. Patient cost inputs: direct healthcare costs, non-healthcare costs such as dependent-living accommodations 3. Caregiver cost inputs: productivity loss from direct caregiving or work lost.	1. Base case ICER: $183,000 (societal)-$192,000 (healthcare) 2. Base case ICER with inclusion of caretaker QALYs: $74,000 (societal)-$107,000 (healthcare)
Boustani 2022 [4]	**Population:** Patients with mild cognitive impairment from AD or mild AD **Perspective:** Healthcare, societal	1. Hypothetical agent + supportive care 2. Supportive care	Cost Utility	1. Treatment effect: 30% reduction in risk of transition from mild AD to more severe states 2. 3 treatment strategies: test and discontinue at 40% clearance of AB deposits, fixed for total of 18 months, continuous until development of severe AD 3. 5 health states based on disease severity 4. All treatment strategies discontinued upon development of severe AD	1. Annual treatment cost at $47,488 then $59,360 from year 2 2. Key cost inputs: direct healthcare costs, long-term care cost, caregiver productivity loss, treatment admin costs, increased monthly healthcare and societal costs with increased disease severity 3. $275,177 of total incremental cost ($285,165) under the healthcare perspective attributed to treatment cost alone	1. Base case ICER (healthcare): $125,631, $157,288, $612,354 based on treatment strategy (test and discontinue, fixed, continuous) 2. Base case ICER (societal): $94,098, $125,201, $573,776

Conclusion

- **Current evidence suggests that passive immunotherapies are not cost effective at their proposed prices.**
- **Almost every passive immunotherapy's price exceeds its value-based price using WTP thresholds between $50,000-$200,000.**
- **Out of all the interventions, Lecanemab's proposed price was most closely aligned with its value-based price range of $9,249-$38,053**
- **ICER values for hypothetical agents were most sensitive to treatment efficacy, suggesting that future disease modifying therapies must be highly efficacious to offset their high-projected cost and be considered cost effective.**